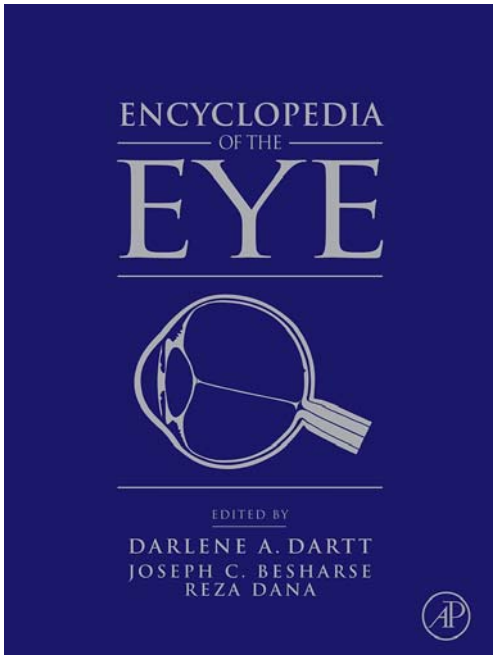

Sebag J Vitreous Anatomy, Aging, and Anomalous Posterior Vitreous Detachment. In: Darlene A. Dartt, editor. Encyclopedia of the Eye, Vol 4. Oxford: Academic Press; 2010. pp. 307-315.

Vitreous Anatomy, Aging, and Anomalous Posterior Vitreous Detachment

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Glossary

Anomalous posterior vitreous detachment – The result of vitreous gel liquefaction without concurrent dehiscence at the vitreo-retinal interface.
Hyalocytes – Mononuclear phagocytes embedded within the posterior vitreous cortex.
Pharmacologic vitreolysis – The use of drugs (enzymes and nonenzymatic agents) to induce gel liquefaction (liquefactants) and dehiscence at the vitreo-retinal interface (interfactants) resulting in prophylactic posterior vitreous detachment (PVD).
Posterior vitreous cortex – The outer shell of the vitreous with a higher density of collagen fibrils and hyaluronan than elsewhere in the vitreous body.
Synchisis – Liquefaction of the gel vitreous.
Syneresis – Collapse of the gel vitreous that results from profound synchisis.
Vitreoschisis – Splitting of the posterior vitreous cortex that results from anomalous PVD that leaves the outermost layer of vitreous attached to the retina, usually in the macula.

Invisible by design (**Figure 1**), vitreous was long unseen as an important part of the eye. In recent years, however, the roles of vitreous in ocular physiology and the pathobiology of various retinal diseases have been increasingly appreciated. As a result, the contribution of vitreous to blindness is being treated with ever-evolving therapeutic modalities, for the most part surgical. The future, however, will see the use of pharmacologic agents for therapy and prevention. To do so successfully requires an understanding of vitreous anatomy and biochemistry as well as an appreciation of how these change with aging and disease. In particular, many retinal diseases can now be conceived as anomalies in the process of posterior vitreous detachment (PVD). This unifying concept of vitreo-retinal diseases is known as anomalous PVD.

Vitreous Anatomy

Vitreous Body

In an emmetropic adult human eye (**Figure 2**), vitreous is approximately 16.5 mm in axial length, with a depression just posterior to the lens (patellar fossa). The hyaloideocapsular ligament (of Weiger) is the annular region 1–2 mm in width and 8–9 mm in diameter where vitreous is attached to the posterior lens. Erggelet's or Berger's space is at the center of the hyaloideocapsular ligament. Arising from this space and coursing posteriorly through the central vitreous is Cloquet's canal – the former site of the hyaloid artery in the primary vitreous. The former lumen of the artery is an area devoid of vitreous collagen fibrils, surrounded by multi-fenestrated sheaths that were previously the basal laminae of the hyaloid artery wall. Posteriorly, Cloquet's canal opens into a funnel-shaped region anterior to the optic disk known as the area Martegiani.

Dissection of the outer layers of the eye (sclera, choroid, and retina) can be performed and the naked vitreous body can be maintained intact and attached to the anterior segment of the eye (**Figure 1**). Studies have identified that within the adult human vitreous there are fine, parallel fibers coursing in an anteroposterior direction (**Figure 3**). These fibers, which probably represent bundles of vitreous collagen fibrils, attach into the vitreous base where they splay out anterior and posterior to the ora serrata. As the peripheral fibers course posteriorly, they are circumferential with the vitreous cortex, while central fibers undulate in a configuration parallel with Cloquet's canal. The fibers are continuous and do not branch. Posteriorly, these fibers attach into the posterior vitreous cortex, but not the retina.

Ultrastructural studies have demonstrated that vitreous collagen tends to be organized into bundles of parallel fibrils (**Figure 4**). It has been hypothesized that, initially, the collagen fibrils within these bundles are spaced apart by the chondroitin sulfate chain of type IX collagen, but with aging the chondroitin sulfate is lost and there is progressive aggregation of the fibrils leading to the formation of thick fibers. Eventually, the fibers attain sufficiently large proportions that they can be visualized *in vitro* (**Figures 3** and **4**) and clinically. The areas adjacent to these large fibers have a low density of collagen fibrils in association with hyaluronan (HA) molecules and, therefore, do not scatter light as intensely as the larger bundles of aggregated collagen fibrils. Furthermore, these adjacent areas offer relatively little resistance to bulk flow through vitreous, since they are largely occupied by hydrated HA.

Vitreous Base

The vitreous base is a three-dimensional zone that extends 1.5–2 mm anterior to the ora serrata, 1–3 mm posterior to the ora serrata, and several millimeters into the vitreous

body itself. The vitreous base posterior to the ora serrata varies in width depending on age. More than half of the population over 70 years of age have a posterior vitreous base wider than 1.0 mm. The width increases with increasing age to nearly 3.0 mm, bringing the posterior border of the vitreous base closer to the equator. This widening of the vitreous base is most prominent temporally. It has been proposed that the intra-retinal synthesis of collagen fibrils that penetrate the internal limiting lamina of the retina and splice with vitreous collagen fibrils, which may explain the increased vitreo-retinal adhesion at the vitreous base, traction, and retinal tears/detachment.

Vitreous Cortex

The vitreous cortex is defined as the peripheral shell of the vitreous body that courses forward and inward from the anterior vitreous base to form the anterior vitreous cortex, and posterior from the posterior border of the vitreous base to form the posterior vitreous cortex (**Figure 5**).

The anterior vitreous cortex, also called the anterior hyaloid face, begins about 1.5 mm anterior to the ora serrata. Here, the vitreous collagen fibrils are parallel to the surface of the cortex and are densely packed with looser collagen-fibril packing in the subjacent vitreous, giving the appearance of lamellae. The anterior vitreous cortex varies in thickness from 800 to 2000 nm with connections to the loose fibrils in the anterior vitreous and multiple interconnections with a branching fibrillar network in the posterior chamber.

The posterior vitreous cortex is 100–110 μm thick and consists of densely packed collagen fibrils. The organization of these collagen fibrils is lamellar, presenting a sheet-like appearance on immunohistochemistry (**Figure 6**). These potential tissue planes are important as sites of tissue separation during PVD (see Section Vitreoschisis) as well as during surgery while peeling membranes off the macula.

Hyalocytes (**Figure 7**) are bone marrow-derived cells widely spread apart in a single layer situated 20–50 μm from the retina in the posterior vitreous cortex and basal vitreous. The highest density of hyalocytes is in the region of the vitreous base, followed next by the posterior pole, with the lowest density at the equator.

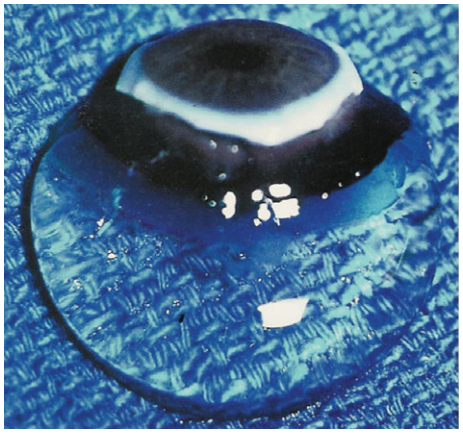

Figure 1 Human vitreous structure in a 9-month-old child.

Vitreoretinal Interface

There is a basal lamina on the inner surface of the retina to which the cortical and basal vitreous are attached. The basal lamina posterior to the ora serrata, known as the internal limiting lamina (ILL) of the retina, is actually the basement membrane of retinal Müller cells. Immediately

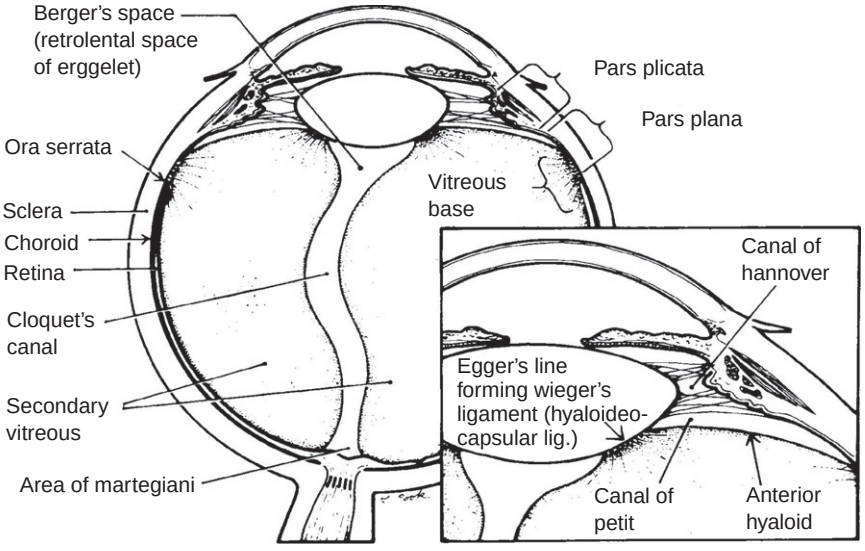

Figure 2 Schematic diagram of vitreous anatomy.

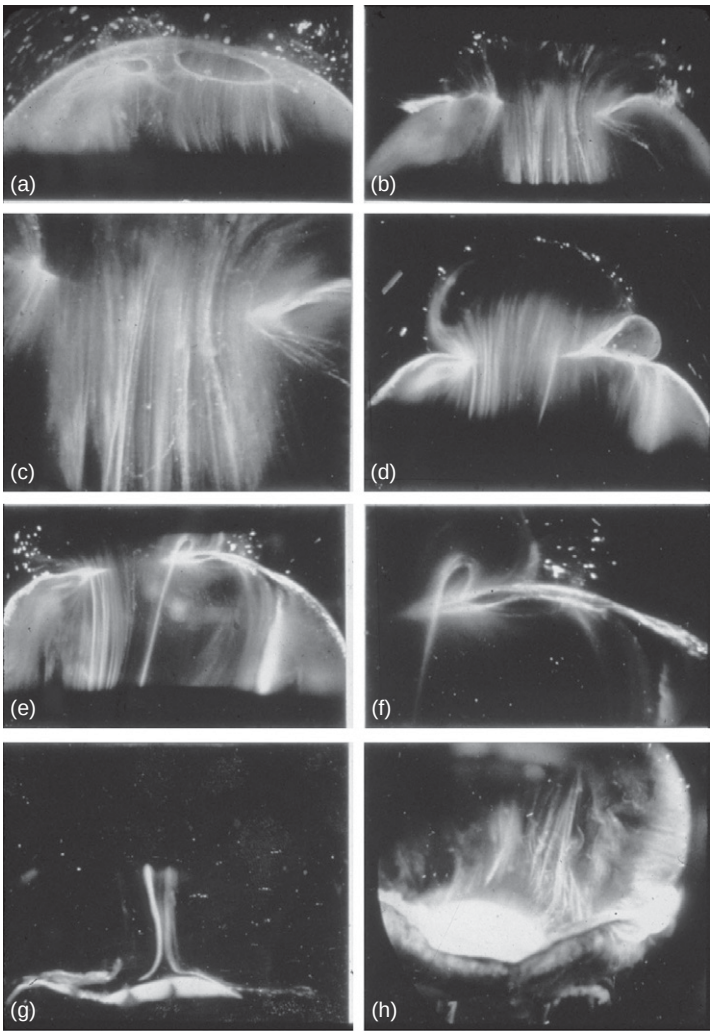

Figure 3 Dark-field slit-lamp microscopy of human vitreous. (a) Left eye of a 52-year-old man. The prepapillary hole in the vitreous cortex is to the left. (b) A 57-year-old man in whom a large bundle of prominent fibers is seen coursing anteroposteriorly and entering the preretinal space through the premacular vitreous cortex. (c) Same view as upper right at higher magnification. (d) A 53-year-old woman in whom there is posterior extrusion of vitreous out the prepapillary hole (to the right) and premacular (large extrusion to the left) vitreous cortex. Fibers course anteroposteriorly in the central vitreous and out into the preretinal, space. (e) Same specimen as second row right. A large fiber courses posteriorly from the central vitreous and inserts into the premacular vitreous cortex. (f) Same view as (e) at higher magnification. The curvilinear appearance is due to traction by vitreous extruding into the retro-cortical space. Because of its attachment to the posterior vitreous cortex, the fiber arcs back to its point of insertion. (g) Cloquet's canal is seen in this 33-year-old woman, forming the retro-lental space of Berger. (h) A 57-year-old man in whom the lens are surrounded by fibers coursing anteroposteriorly that insert into the vitreous base. These fibers splay out to insert anterior and posterior to the ora serrata.

adjacent to the Müller cell is a lamina rara (0.03–0.06 μm thick) that demonstrates no species variations, nor changes with topography or age. The lamina densa (i.e., the basement membrane itself) is thinnest at the fovea (0.01–0.02 μm) and disk (0.07–0.1 μm). It is thicker elsewhere in the posterior pole (0.5–3.2 μm) than at the equator or vitreous base. The existence of lamellae within the ILL has relevance to the pathophysiology and surgical repair of macular holes.

The vitreous is known to be most firmly attached at the vitreous base, at the disk and macula, and over retinal blood vessels. The posterior aspect (retinal side) of the ILL demonstrates irregular thickening the farther posteriorly one goes from the ora serrata. So-called attachment plaques between the Müller cells and the ILL have been described in the basal and equatorial regions of the fundus but not in the posterior pole, except for the fovea. It has been hypothesized that these plaques develop in response to vitreous traction on the retina. The thick ILL in the posterior pole dampens the effects of this traction except at the fovea where the ILL is thin. The thinness of the ILL and the purported presence of attachment plaques at the central macula could explain the predisposition of this region to changes induced by traction.

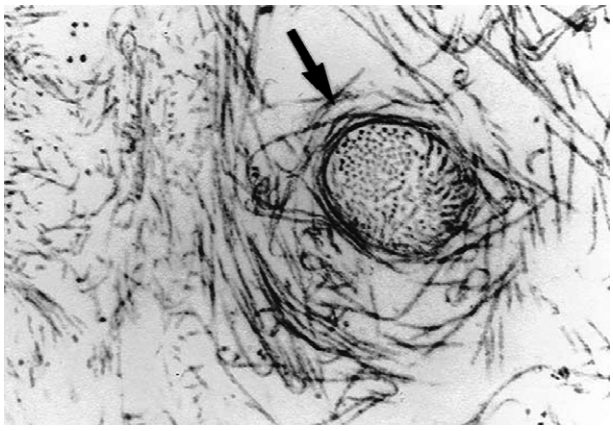

Figure 4 Transmission electron microscopy of human vitreous. Transmission electron microscopy of human vitreous demonstrates collagen fibrils organized in a bundle of parallel fibrils as seen here in cross-section.

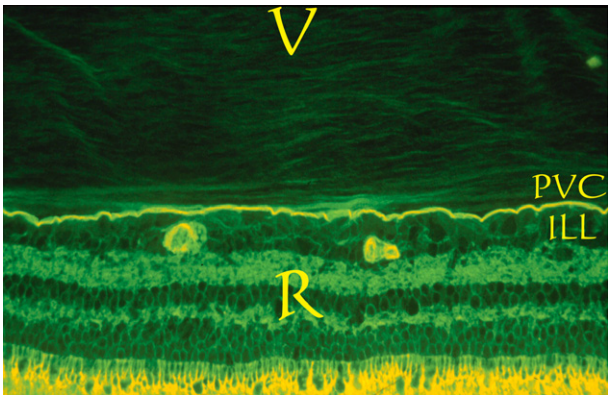

Figure 6 Immunohistochemistry of the human vitreoretinal interface demonstrates intense staining of the internal limiting lamina (ILL) with anti-ABA antibodies. This lectin binding is also evident, although less intense, in the lamellae of the posterior vitreous cortex (PVC, above the bright line in the middle – which is the ILL). Courtesy of Greg Hageman, PhD, University of Iowa.

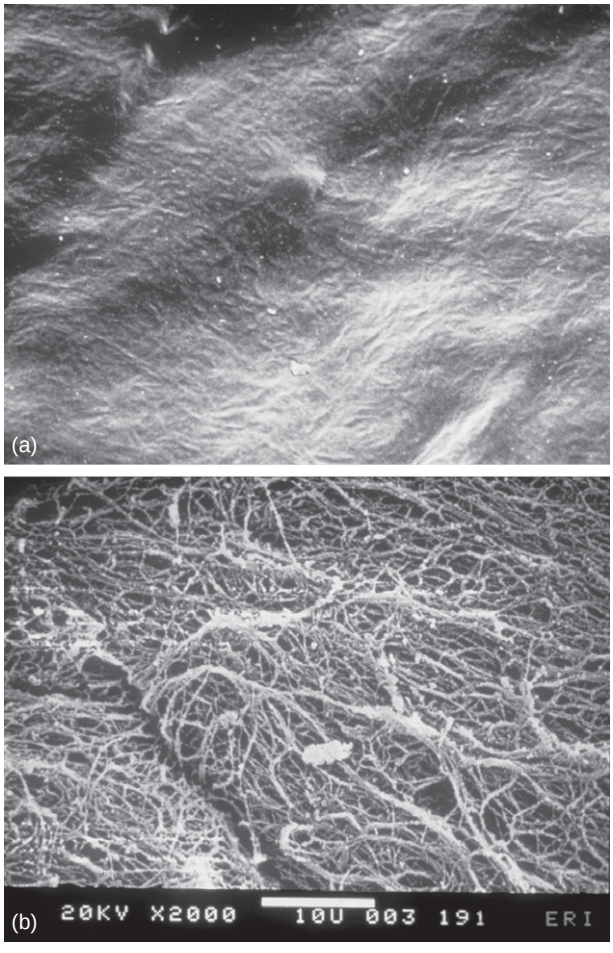

Figure 5 Scanning electron microspcopy of human vitreo-retinal interface. (a) Scanning electron microscopy of posterior aspect of posterior vitreous cortex and (b) anterior surface of internal limiting lamina of retina.

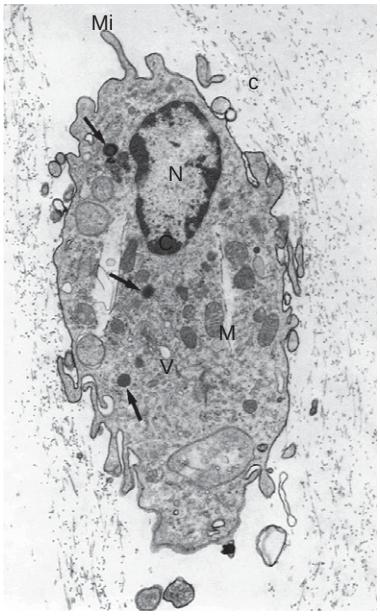

Figure 7 Ultrastructure of the human hyalocyte. A mononuclear cell is seen embedded within the dense collagen fibril (black C) network of the vitreous cortex. There is a lobulated nucleus (N) with dense marginal chromatin (white C). In the cytoplasm there are mitochondria (M), dense granules (arrows), vacuoles (V), and microvilli (Mi) (×1670). Courtesy of JL Craft and DM Albert, Harvard Medical School, Boston.

Aging Changes

Throughout life, there are changes in vitreous structure (Figure 8). During late prenatal and early postnatal stages, there are no structures within the vitreous body other than the remnants of the hyaloid artery oriented

toward the prepapillary region (Figure 8, top row). The vitreous body is relatively small and has an overall dense appearance with marked density at the outermost shell corresponding to the vitreous cortex. The generalized density of the vitreous likely relates to the fact that, at this stage of development, collagen and proteoglycan(s) other than HA are the principal structural components. HA synthesis begins following birth, increasing transparency by the aforementioned mechanisms. During childhood, only the vitreous cortex scatters incident light and thus appears dense upon dark-field slit microscopy. There are no visible fibers within the vitreous until middle age (Figures 3 and 8 – middle row). During old age, these fibers become thickened and tortuous, associated with many pockets of liquid vitreous and a collapsed (syneretic) appearance (Figure 8, bottom row). These changes are the result of age-related biochemical alterations in the composition and organization of the molecular components that simultaneously result in vitreous liquefaction and fiber formation. Pockets of liquid vitreous have classically been called lacunae. In addition to having a low density of collagen during youth, the central vitreous is the first region to undergo liquefaction during middle age. A large autopsy study of human eyes found that more than one-half of the vitreous was liquefied in 25% of persons in the age range of 40–49 and that this increased to 62% of individuals in the age range of 80–89. In another study, ultrasonography was used *in vivo* to detect echoes from gel–liquid interfaces in 444 normal human eyes and observed echoes in 5% of young persons, in more than half of those in the age range of 51–60, and in more than 80% of persons over 60 years. However, there is evidence of liquid vitreous following the age of 4 years and, by the time the human eye reaches its adult size (age range: 14–18 years), approximately 20% of the total vitreous volume consists of liquid vitreous.

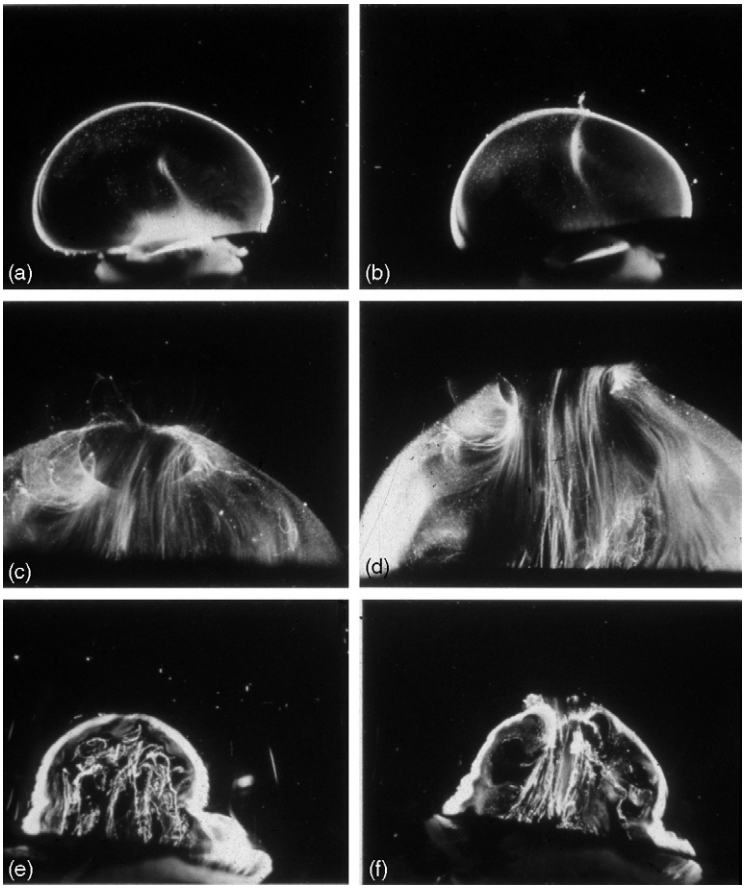

Figure 8 Changes caused by aging in human vitreous structure. (a, b) Dark-field slit microscopy of the posterior and central vitreous in a 33-week-old human embryo shows considerable light scattering arising from the vitreous cortex, due to densely packed collagen fibrils. In the central vitreous is the remnant of the hyaloid artery oriented toward the prepapillary posterior vitreous cortex. This structure is destined to become Cloquet's canal. (c, d) Vitreous structure in adults is characterized by macroscopic fibers with an antero-posterior orientation, inserting into the vitreous base. (e, f) In old age, there is aggregation of the fibers into tortuous structures with adjacent pockets of liquid vitreous that ultimately form lacunae (left side of photograph on right, bottom panel).

Posterior Vitreous Detachment (PVD)

True PVD (Figure 9) is a separation between the posterior vitreous cortex and the ILL of the retina. PVD can be localized, partial, or total (throughout the entire posterior pole up to the posterior border of the vitreous base). Although there are various methods for examining the vitreous, it is difficult to accurately determine the presence or absence of true PVD both in research and clinical settings. The future, however, may see improvements in this diagnostic acumen through the use of new diagnostic technologies, such as dynamic light scattering.

Epidemiology of PVD

In clinical studies, the incidence of PVD has been purported to be 53% in persons older than 50 and 65% in those older than 65. Autopsy studies revealed an incidence of 27–51% in the seventh decade and 63% in the eighth decade. It is not certain, however, that these are not overestimates owing to the suspension-in-air methods employed in these postmortem studies. PVD is more common in myopic patients, occurring 10 years earlier than in emmetropia and hyperopia. This is likely the result of myopic vitreopathy Cataract extraction in myopic patients introduces additional effects. In one study, PVD was present in 102 of 103 myopic eyes with myopia greater than −6 D that had undergone cataract extraction (presumably intracapsular).

There is a higher incidence of PVD in women than men, a finding that may be due to hormonal changes following menopause. This hypothesis is supported by findings that glycosaminoglycan synthesis can be influenced by a variety of hormones. There is also evidence that sex hormones can affect glycosaminoglycans metabolism, for example, there are variations in the concentration of HA following hormonal treatment. The vitreous HA concentrations in men ($120.89 \pm 75.44\,\mu g\ ml^{-1}$) is significantly greater than in women ($79.53 \pm 48.17\,\mu g\ ml^{-1}$; $p < 0.01$). This may be related to low estrogen levels in postmenopausal women and may explain why PVD is more common in women than men. Furthermore, all these lines of evidence support the concept that insufficient or abnormal HA destabilizes the gel state of vitreous contributing to liquefaction and PVD.

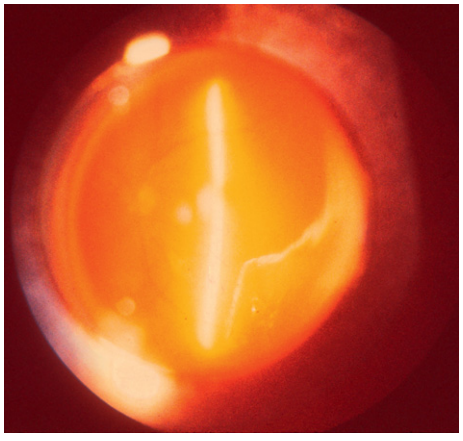

Figure 9 Posterior vitreous detachment. Preset lens biomicroscopy of the left eye in a patient with a complete PVD. The optic disk and retinal vessels can be seen to the left and the detached posterior vitreous cortex, which is brightly illuminated by the slit beam, is located to the right. Courtesy of C. L. Trempe, MD, Boston.

Pathogenesis of PVD

Several studies have shown that PVD begins at the posterior pole. PVD results from concurrent changes within the vitreous body and at the vitreoretinal interface. Whether due to age-related changes in collagen structure, HA conformation and/or concentration, light-induced or metabolically derived free radicals, hormonal effects, or combinations of all these factors, there is a disruption of the normal collagen–HA association transforming the gel vitreous to liquid. Dissolution of the ILL–vitreous cortex adhesion at the posterior pole allows this liquid vitreous to dissect a retro-cortical plane, resulting in collapse of the vitreous body. Further studies on the nature of HA–collagen interactions and the forces underlying posterior vitreous cortex–ILL adhesion should help to further identify the changes that result in PVD. Elucidating these mechanisms may enable the development of techniques by which liquefaction and PVD could be induced or prevented, depending on the clinical circumstances.

Sequela of PVD

In youth, the vitreous body is normally clear and has little or no effect on glare sensitivity. In old age, the aggregation of vitreous collagen fibrils into thick, irregular, visible fibers (Figures 3 and 8) can induce glare sensitivity, which may be subjectively bothersome. Furthermore, the high incidence of PVD in old age may also induce glare owing to scattering of light by the dense collagen fibril network in the posterior vitreous cortex (Figure 5). A group of individuals in whom glare diskomfort is a common complaint comprises patients who have undergone scleral buckling surgery for rhegmatogenous retinal detachment. The complaint of glare appears to be due to postoperative vitreous turbidity and not due to a change in the threshold sensitivity of retinal receptors. Scleral buckle surgery adds to the preexisting vitreous inhomogeneity by inducing temporary dysfunction of the blood ocular barriers – causing an influx of serum proteins and other macromolecules, as well as creating an inflammatory response and influx of cellular elements.

Floaters are the most common complaint of patients with PVD. These usually result from entopic phenomena caused by condensed vitreous fibers, glial tissue of epi-papillary origin, and/or intravitreal blood. Floaters move with vitreous displacement during eye movement and scatter incident light, casting a shadow on the retina that is perceived as a gray, hair-like or fly-like structure. In an autopsy series of cases with complete PVD, 57% had glial tissue on the posterior vitreous cortex and, in a study of cases of floaters, glial tissue was detected on the posterior vitreous cortex in 83% of patients.

Anomalous PVD

PVD is innocuous when gel liquefaction, which causes vitreous body destabilization – develops in tandem with dehiscence at the vitreo-retinal interface. If the degree of vitreo-retinal dehiscence is sufficient to allow syneresis (collapse), the vitreous body pulls away from the retina without untoward sequela (**Figure 9**). When there is insufficient vitreo-retinal dehiscence, the destabilized, liquefied vitreous cannot pull away cleanly, resulting in the development of anomalous PVD. There are various sequela to anomalous PVD (**Figure 10**).

When the entire (full-thickness) posterior vitreous cortex separates from the macula, but induces peripheral vitreo-retinal traction, retinal tears and detachments are induced. Posterior full-thickness traction can pull on the macula and induce vitreo-macular traction syndrome or place traction upon the optic disk, exacerbating neovascularization in proliferative diabetic retinopathy or other ischemic retinopathies, inducing vitreous hemorrhage, or resulting in vitreo-papillary traction syndromes. Partial PVD with splitting of the posterior vitreous cortex (vitreoschisis) may be the first event in macular pucker and macular hole pathogenesis.

Retinal Tears

Autopsy studies found that PVD is associated with retinal breaks in 14.3% of all cases. A degree of vitreous hemorrhage occurs in 13–19% of cases with PVD and, when patients suffer a severe vitreous hemorrhage that obscures the view of the fundus on ophthalmoscopy, there is a high-incidence of retinal tears (67%) and retinal detachments (39%).

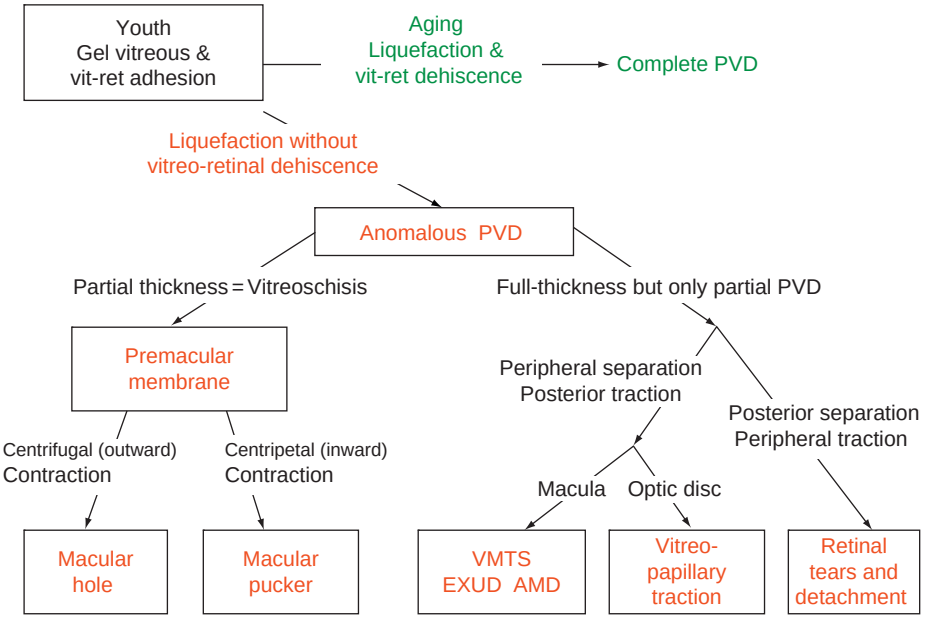

Figure 10 Schematic diagram of anomalous PVD. This schematic diagram demonstrates the various possible manifestations of anomalous PVD. When gel liquefaction and weakening of vitreoretinal adhesion occur concurrently, the vitreous separates away from the retina without sequela (top of diagram). If the separation of vitreous from retina is full-thickness but incomplete, there can be different forms of partial PVD (right side of diagram). Posterior separation with persistent peripheral vitreoretinal attachment can induce retinal breaks and detachments. Peripheral vitreoretinal separation with persistent full-thickness attachment of vitreous to the retina posteriorly can induce traction upon the macula, known as the vitreo-macular traction syndrome (VMTS). This phenomenon appears to be highly associated with exudative age-related macular degeneration (AMD). Persistent attachment to the optic disk can induce vitreo-papillopathies and also contribute to neovascularization and vitreous hemorrhage in ischemic retinopathies. If, during PVD, the posterior vitreous cortex splits (vitreoschisis), there can be differences depending upon the level of the split. Vitreoschsis anterior to the level of the hyalocytes leaves a relatively thick, cellular membrane attached to the macula. Inward (centripetal) contraction of this membrane induces macular pucker. If the split occurs at a level posterior to the hyalocytes, the remaining premacular membrane is relatively thin and hypocellular. Outward (centrifugal) tangential traction can induce a macular hole.

Vitreo-Macular Traction Syndrome

Vitreo-macular traction syndrome (VMTS) results when there is peripheral PVD but persistent attachment of full-thickness (i.e., not split) posterior vitreous cortex to the macula. This induces axial traction upon the macula with thickening due to both the effects of traction as well as edema. Full-thickness vitreo-macular adhesion may also be important in patients with age-related macular degeneration (AMD). Recent studies have identified that true PVD is protective against wet AMD, while anomalous PVD with persistent vitreo-macular adhesion may promote choroidal neovascularization.

Vitreoschisis

PVD is associated with vitreous cortex remnants at the fovea in 44% of human eyes studied at autopsy with scanning electron microscopy. When these remnants are a layer or sheet of posterior vitreous cortex, the term vitreoschisis is appropriate. On clinical examination, the inner wall of the vitreoschisis cavity may be clinically confused with a PVD when the posterior layer of the split vitreous cortex remains attached to the ILL of the retina.

Ulltrasonography (Figure 11) can, at times, detect the split layers in vitreoschisis – depending upon the thickness of the layers. Vitreoschisis has been detected by ultrasound in 20% of eyes with proliferative diabetic retinopathy and optical coherence tomography detected vitreoschisis in about one-half of patients with macular pucker and macular holes.

Figure 11 Ultrasonography of vitreoschisis. B-scan ultrasound of vitreoschisis in a human demonstrates the inner (I) and outer (P) walls of a split posterior vitreous cortex. The arrow indicates the schisis cavity created by the split.

Macular Pucker

Following vitreoschisis, premacular membranes can contract and cause significant visual impairment and metamorphopsia, sometimes necessitating surgical intervention. Studies of excised tissue have demonstrated the presence of astrocytes and retinal pigmentary epithelium (RPE) cells, but there can likely be other cells that can have similar appearances – such as hyalocytes. It has been hypothesized that macular pucker results when vitreoschisis splits the cortex anterior to hyalocytes leaving this cellular membrane attached to the macula.

Recent studies have identified that nearly one-half of all eyes with macular pucker have more than one site of retinal contraction (Figure 12). There is a higher incidence of intra-retinal cysts and significantly more macular thickening with increasing foci of retinal contraction.

Macular Holes

The precise pathogenesis of macular holes is unknown, although several hypotheses have been presented over the years. Initial theories cited anteroposterior traction by vitreous fibers, while more recent hypotheses incriminate tangential traction upon the macula. Advanced imaging using combined optical coherence tomography and scanning laser ophthalmoscopy has determined that nearly all subjects with macular holes have vitreo-papillary adhesion – suggesting that this might alter the vectors of force upon the macula inducing outward (centrifugal) tangential traction inducing a central hole.

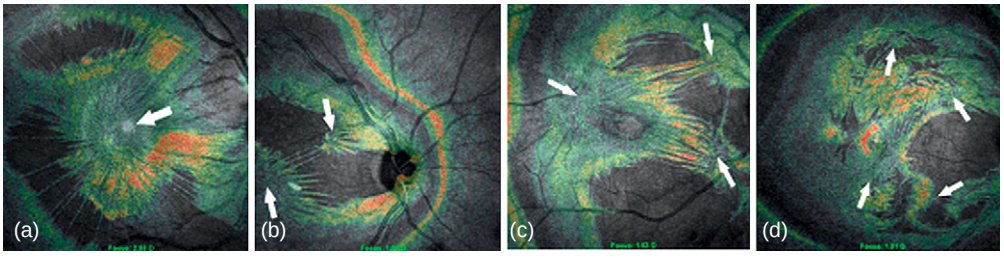

Figure 12 Multi-focal retinal contraction in macular pucker. Superimposed coronal plane OCT images upon the SLO fundus images reveal multi-focality (arrows) in the pattern of macular pucker. (a) 1 pucker center, (b) 2 pucker centers, (c) 3 pucker centers, and (d) 4 puckers centers.

See also: Hyalocytes; Molecular Composition of the Vitreous and Aging Changes; Pharmacological Vitreolysis; The Role of the Vitreous in Macular Hole Formation.

Further Reading

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